

Docket No.: 284057US0PCT

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF: :
RAMON MERCE VIDAL, et al. : EXAMINER: RICCI, C.D.
SERIAL NO.: 10/566,094 :
FILED: OCTOBER 3, 2006 : ART UNIT: 1614
FOR: INDOL-5-YL SULFONAMIDE DERIVATIVES, THEIR PREPARATION AND
THEIR USE 5-HT-6 AS MODULATORS

APPEAL BRIEF

COMMISSIONER FOR PATENTS
P.O. BOX 1450
ALEXANDRIA, VA 22313-1450

SIR:

This is an appeal of Claims 1-14, 18, 19, 46, 47, 74-82, 84-90, 92, and 93 in the above-identified application and the rejections set forth in the Official Action mailed October 1, 2009.

I. Real Party of Interest

The real party of interest is LABORATORIOS DEL DR. ESTEVE S.A., by virtue of the assignment recorded in the U.S. Patent and Trademark Office on October 3, 2006, at reel 018443, frames 0671-0673.

II. Related Appeals and Interferences

Appellants, Appellants' legal representative and their assignee are not aware of any appeals or interferences which will directly affect or be directly affected by or having a bearing on the Board's decision in this appeal.

III. Status of Claims

Claims 1-14, 18, 19, 46, 47, and 74-93 are the only claims pending in the above-identified application.

No claims that have been presented for examination are allowed.

No claims that have been presented for examination are withdrawn from examination.

Claims 83 and 91 that have been presented for examination stand objected to.

Claims 15-17, 20-45, and 48-73 that were presented during prosecution are canceled.

Claims 1-14, 18, 19, 46, 47, and 74-93 are the only elected claims in this application.

Claims 1-14, 18, 19, 46, 47, 74-82, 84-90, 92, and 93 stand rejected.

Claims 1-14, 18, 19, 46, 47, 74-82, 84-90, 92, and 93 are appealed herein.

Claims 1-14, 18, 19, 46, 47, and 74-93 appear in the attached Claims Appendix.

Claims 1 and 9 are the only independent claims in the above-identified application that is subject to appeal.

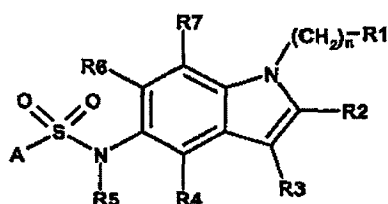
IV. Status of Amendments filed under 37 C.F.R. §1.116

A Request for Reconsideration after final rejection mailed October 1, 2009, was not filed. Each claim that is subject to this appeal has been at least twice rejected. Appellants now appeal the rejections set forth in the final Office Action mailed October 1, 2009.

V. Summary of the Claimed Subject Matter

Independent Claim 1 provides:

A sulfonamide compound of general formula (Ia)



(Ia)

wherein

R¹ represents an -NR⁸R⁹ radical or a saturated or unsaturated, optionally at least mono-substituted, cycloaliphatic radical, which may optionally contain at least one heteroatom as a ring member and/or which may be condensed with a saturated or unsaturated, optionally at least mono-substituted mono- or bicyclic cycloaliphatic ring system, which may optionally contain at least one heteroatom as a ring member,

R², R³, R⁴, R⁶ and R⁷, identical or different, each represent hydrogen, halogen, nitro, alkoxy, cyano, a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical or an optionally at least mono-substituted phenyl radical or an optionally at least mono-substituted heteroaryl radical,

R⁵ represents hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

R⁸ and R⁹, identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

with the proviso that R⁸ and R⁹ are not hydrogen at the same time, and if one of them, R⁸ and R⁹, represents a saturated or unsaturated, linear or branched, optionally at least mono-

substituted C₁-C₄ aliphatic radical, the other one represents a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical with at least five carbon atoms, or

R⁸ and R⁹ together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted heterocyclic ring, which may contain at least one additional heteroatom as a ring member and/or which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, mono- or bicyclic cycloaliphatic ring system which may optionally contain at least one heteroatom as a ring member,

A represents an optionally at least mono-substituted mono- or polycyclic aromatic ring system, which may be bonded via an optionally at least mono-substituted alkylene, alkenylene or alkynylene group and/or which may contain at least one heteroatom as a ring member in one or more of its rings,

and

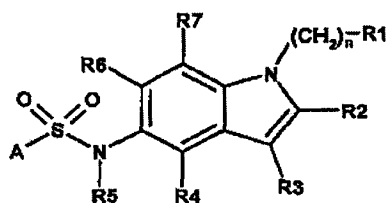
n is 0, 1, 2, 3 or 4;

optionally in form of one of its stereoisomers, its racemate or in form of a mixture of at least two of its stereoisomers, in any mixing ratio, or a salt thereof.

(see original Claim 1, as well as the specification, for example, at page 1, lines 5-16, page 4, line 6 to page 5, line 32, page 13, line 26 to page 21, line 10 (and the corresponding Examples). Claims 2-8, 18, 19, 74-83, and 92 depend from Claim 1 either directly or indirectly.

Independent Claim 9 provides:

A sulfonamide compound of general formula (Ib)



(Ib)

wherein

R¹ represents a -NR⁸R⁹ radical,

R², R³, R⁴, R⁶ and R⁷, identical or different, each represent hydrogen, halogen, nitro, alkoxy, cyano, a saturated or unsaturated, optionally at least mono-substituted, linear or branched aliphatic radical, or an optionally at least mono-substituted phenyl or an optionally at least mono-substituted heteroaryl radical,

R⁵ represents hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

R⁸ and R⁹, identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted, C₁-C₄ aliphatic radical,

A represents an optionally at least mono-substituted mono- or polycyclic aromatic ring system, which may be bonded via an optionally at least mono-substituted alkylene, alkenylene or alkynylene group and/or which may contain at least one heteroatom as a ring member in one or more of its rings,

and n is 0, 1, 2, 3 or 4;

optionally in form of one of its stereoisomers its racemate or in form of a mixture of at least two of its stereoisomers, in any mixing ratio, or a salt thereof.

(see original Claim 9, as well as the specification, for example, at page 6, line 1 to page 7, line 7, page 21, line 12 to page 30, line 13 (and the corresponding Examples)). Claims 10-14, 46, 47, 84-91, and 93 depend from Claim 9 either directly or indirectly.

VI. Grounds of Rejection to be Reviewed on Appeal

1. Claims 1-14, 18-19, 46-47, 74-82, 84-90, and 92-93 stand rejected under 35 U.S.C. §103(a) as being obvious over Merce-Vidal et al (WO 03/042175; English equivalent taken as CA 2466965) in view of Filla et al (WO 02/060871).

VII. Arguments

A. Claims 1-14, 18-19, 46-47, 74-82, 84-90, and 92-93 stand rejected under 35 U.S.C. §103(a) as being obvious over Merce-Vidal et al (WO 03/042175; English equivalent taken as CA 2466965) in view of Filla et al (WO 02/060871). This rejection is untenable and should not be sustained.

Despite previous Appellants' arguments, the Examiner maintains in the Final Office Action mailed October 1, 2009, that the compounds of the present invention differs from the prior art compounds taught by Merce-Vidal et al by a single modification (i.e., is a positional isomer, compounds which *In re Wilder*, 563 F.2d 457 (CCPA 1977) teach are generally of sufficiently close structural similarity to possess similar properties) and that said single modification would have also been *prima facie* obvious in view of Filla et al. Applicants disagree for the reasons that follow:

Case Law: Takeda

As discussed in the response filed by the Appellants on August 21, 2009, the Court of Appeals for the Federal Circuit clearly state in *Takeda Chemical Industries Ltd. v. Alphapharm Pty. Ltd.*, 83 USPQ2d 1169 (Fed. Cir. 2007) that in order to find a *prima facie* case of unpatentability, a showing that the "prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention" was also required (*Takeda* at 1174, citing *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992); *In re Dillon*, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1990); *In re Grabiak*, 769 F.2d 729, 226 USPQ 870 (Fed. Cir. 1985); *In re Lalu*, 747 F.2d 703, 223 USPQ 1257 (Fed. Cir. 1984)).

Moreover, as clearly stated by *Takeda* at 1174, the Court squarely addressed the test for *prima facie* obviousness enunciated by the Supreme Court in *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 [82 USPQ2d 1385](2007) in the context of chemical compounds:

That test for *prima facie* obviousness for chemical compounds is consistent with the legal principles enunciated in *KSR*.² While the *KSR* Court rejected a rigid application of the teaching, suggestion, or motivation ("TSM") test in an obviousness inquiry, the Court acknowledged the importance of identifying "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does" in an obviousness determination. *KSR*, 127 S. Ct. at 1731. Moreover, the Court indicated that there is "no necessary inconsistency between the idea underlying the TSM test and the *Graham* analysis." *Id.* As long as the test is not applied as a "rigid and mandatory" formula, that test can provide "helpful insight" to an obviousness inquiry. *Id.* Thus, *in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound.* (emphasis added)

Appellants assert that the **Examiner's arguments appearing in the Final Office Action are not proper to establish a *prima facie* obviousness rejection.** In this regard,

instead of showing the above-mentioned requisite reason, the Final Office Action is mainly aimed to differentiate the instant case from *Takeda*.

In view of the foregoing, Appellants submit that the present invention is not obvious in view of Merce-Vidal et al or Filla et al as these references fail to provide the requisite reason that would have led a chemist to modify the compounds disclosed therein in the manner necessary to arrive at the claimed compounds. Thus, Merce-Vidal et al and Filla et al fail to support even a *prima facie* case of obviousness.

Tryptamine-like structure

The Examiner contends that the instant case is distinguishable from *Takeda* in that the prior art compound taught by Merce-Vidal et al differs from the instantly claimed compound in only **one** respect (i.e., ring walking the moiety from position 3 to position 1) whereas in *Takeda* the compounds differed in **two** respects (i.e., ring walking and homologation).

Furthermore, even assuming that the “ring walking” encompasses two changes (i.e. “the introduction ... at position 1” and “the elimination ... at position 3” of the substituent (Appellant Arguments filed August 21, 2009), the Examiner contends that the instant case would be still distinguishable from *Takeda* in that the prior art compound taught by Merce-Vidal et al differs from the instantly claimed compound in only **two** respect (i.e., ring walking the moiety from position 3 to position 1 – which involves two changes) whereas in *Takeda* the compounds differed in **three** respects (i.e., ring walking, which involves two changes, and homologation).

Further, asserted claim 1 of the '777 patent in *Takeda* recites a formula general wherein the ethyl-substituted pyridyl ring is located at one of four available positions on the pyridyl ring, generating 3-, 4-, 5-, and 6-ethyl compounds. Accordingly, the court allowed

claim 1 in spite of the 6-ethylpyridyl derivative would differ from the prior art compound be in only one respect (homologation) [compound b possesses a pyridyl ring in which a methyl (CH₃) group is attached to the 6-position].

Regardless of the specific number of differences in the present case as compared to Takeda, the point at issue is that Merce-Vidal et al provides no hint as to moving the amino moiety or the N-containing cycloaliphatic ring to the 1-position of the indole ring without losing affinity for the 5-HT₆ receptor. Neither would the skilled person have been motivated to change the -(CH₂)_n-R² moiety of Merce-Vidal et al to position 1 in view of the teaching of Filla et al.

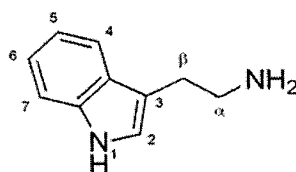
Moreover, as discussed previously, in the instant case it is of the utmost importance to identify that the change of the substituent of the compounds disclosed in Merce-Vidal et al from position 3 to position 1 ("ring walking") in order to arrive at the claimed compounds involves two changes as the second one disrupts the so characteristic tryptamine-like structure. In concrete, said ring walking comprises the following modifications:

- the introduction of a precisely defined substituent containing nitrogen at position 1;
- but also, and very importantly, the elimination of this specific and mandatory substituent from position 3 in Merce-Vidal et al.

Concerning the first change, it is not obvious that the introduction of an aminoalkyl substituent at position 1 would give compounds with 5-HT₆ activity. As already pointed out in previous responses, Filla et al do not show a single example of the biological activity of the indole compounds described therein. Further, the substituent at position 1 in Filla et al is not an aminoalkyl as defined in the instantly claimed compounds. Thus, the skilled artisan would find not reasonable motivation or expectation of success in either Filla et al and/or Merce-Vidal et al to introduce a alkylamino substituent at position 1 of the indole ring.

Concerning the second change, Appellants submit that the skilled artisan would not consider that the elimination of the specific substituent at position 3 in the compounds of Merce-Vidal et al could give compounds with 5-HT₆ activity.

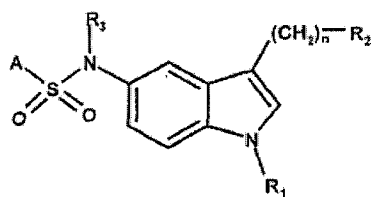
In this regard, Appellants again emphasize the "tryptamine-like" argument as, in contrast to the indole compounds disclosed in Merce-Vidal et al and Filla et al, the compounds of the present invention do not have a tryptamine-like structure.



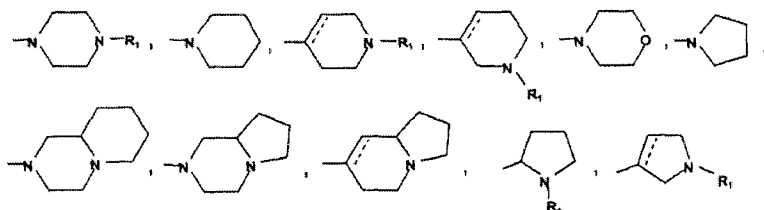
tryptamine

As may be observe, the general formulae described both in Merce-Vidal et al and in Filla et al are 2-aminoalkyindoles:

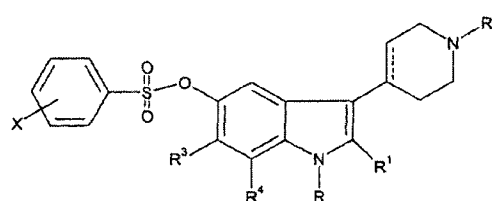
Merce-Vidal et al.



R₂ represents -NR₄R₅ or a group with formula:

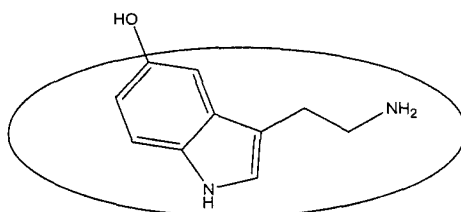


Filla et al.



Appellants have previously submitted appropriate evidence of that i) the compounds disclosed in the cited references are based on a tryptamine framework and ii) it is widely

known in the state of the art that said tryptamine framework is common in numerous serotonin receptor ligands. Indeed, serotonin (5-hydroxytryptamine) presents the following structure:



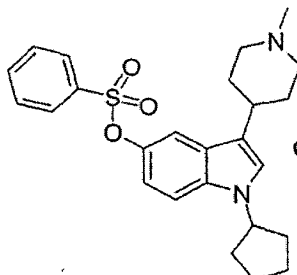
As stated for instance in Sophie-Isabelle Bascop et al., *Arkivoc* **2003** 46-61, 2(3)-aminoalkyl indoles, not only tryptamine derivatives but also homotryptamine and isotryptamine related derivatives, have attracted considerable interest as potent and selective serotonin receptor ligands, such as 5-HT₆ receptor. Some documents reporting this structure-activity relationship are shown hereinunder:

- Richard A. Glennon et al., “2-Substituted Tryptamines: Agents with Selectivity for 5-HT₆ Serotonin Receptors”, *J. Med. Chem.*, **2000**, 43 (5), pp 1011–1018.
- Yuching Tsai et al., “N1-(Benzenesulfonyl)tryptamines as novel 5-HT₆ antagonists”, *Bioorganic & medicinal chemistry letters* **2000**, vol. 10, no 20, pp. 2295-2299.
- US 7098233, “5-halo-tryptamine derivatives used as ligands on the 5-HT₆ and/or 5-HT₇ serotonin receptors”.

Therefore, in the instant case a person of ordinary skill in the art would not have found apparent to move the amino moiety or the N-containing cycloaliphatic ring to the 1-position of the indole ring as discussed above because such movement would involve the rupture of the tryptamine-like structure, which was considered essential for the activity as shown in Merce-Vidal et al and in Filla et al.

However, and surprisingly, the Examiner maintains that Example 28 in Filla et al (page 67) does not appear to show a tryptamine-like structure since it possesses a 3-

aminocycloalkylindole structure (i.e. a tertiary amine), but not a 3-aminoalkylindole basic structure (i.e. a primary amine).



Example 28, Filla et al

Appellants disagree and respectfully state that the tryptamine structure is clearly present in Example 28 of Filla et al, as may be appreciate from just the prior art references cited above. It is to be noted in this respect for instance that compounds 6-16 disclosed in Glennon et al (*Journal of Medicinal Chemistry*, 2000, Vol. 43, No. 5), or compounds 5-16 disclosed in Tsai et al (*Bioorganic & medicinal chemistry letters* **2000**, vol. 10, no 20, pp. 2295-2299) in spite of being tertiary amines, are considered as tryptamine analogues.

Routine drug optimization process

In the Final Office Action mailed October 1, 2009, the Examiner also contends that Appellants have not provide evidence to suggest that the ring walking was not a routine step in the drug optimization process at the time the instant invention was made (as was the case in *Takeda*; see page 1360).

As response Appellants state according to *Takeda* the concept of “routine steps in the drug optimization process” must be associated with the existence of any motivation in the prior art to make the specific molecular modifications to the compounds disclosed in the prior art that are necessary to achieve the claimed compounds. Therefore, the change of the substituent of the compounds disclosed in Merce-Vidal et al from position 3 to position 1

("ring walking") does not represent a routine step in the drug optimization process since there is nothing in the prior art to suggest performing said ring walking.

Combination of Merce-Vidal and Filla

Further, the Examiner contends that the specific molecular modifications necessary to achieve the claimed invention are motivated in further view of Filla et al.

As has been widely discussed, the disclosure of Filla et al does not provide any basis to motivate the skilled person to change the $-(CH_2)_n-R^2$ moiety of Merce-Vidal et al to position 1 of the indole ring, much less generate a reasonable expectation of success as alleged by the Examiner.

The Examiner's attention is first drawn to the fact that position 3 on the indole ring in Merce-Vidal et al is substituted by a $-(CH_2)_n-R^2$ moiety, wherein R^2 represents $-NR^4R^5$ or a specific non-aromatic nitrogen containing ring selected from a list of 11 different chemical formulae. On the contrary, position 1 on the indole in Filla et al does not contain the possibility of an amino-alkyl chain nor a non-aromatic nitrogen containing ring. Further, position 5 on the compounds of Filla et al in comparison with Merce-Vidal et al is occupied by a different chemical group (sulfonic acid vs. sulfonamide). Accordingly, both Merce-Vidal et al and Filla et al disclose indole compounds differing not only in the position of their substituents, but also in their nature.

Therefore, the skilled artisan, starting from Merce-Vidal et al would not have any basis and/or motivation to change the $-(CH_2)_n-R^2$ moiety to position 1, because this implies going beyond the teaching of both Merce-Vidal et al and Filla et al, as well as ignoring the recommendations of Filla et al for the specific substituents that are to be used at position 1 in

order to obtain compounds which are antagonists of the 5-HT₆ receptor. The definition of R in Filla et al is

“R is hydrogen, C1-C6 alkyl, substituted C1-C6 alkyl, C3-C6 cycloalkyl, C1-C6 alkylsulfonyl, phenylsulfonyl, substituted phenylsulfonyl, naphthylsulfonyl, benzylsulfonyl, or substituted benzylsulfonyl;”

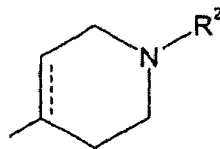
According to Filla et al (page 11, lines 31-37) preferred antagonists of 5-HT₆ receptor are compounds of formula I wherein **R** is hydrogen or C₁-C₆ alkyl, R and R¹ are taken together to form -CH₂-CH₂-CH₂- or -CH₂-CH₂-CH₂-CH₂-, or R and R⁴ are taken together to form -CH₂-CH₂-CH₂-.

From the foregoing, it is clear that the substituent R at position 1 on the indole in Filla et al does not include the groups disclosed in Merce-Vidal et al for position 3.

Thus, in the unlikely event that the skilled artisan would consider modifying the compounds of Merce-Vidal et al in order to introduce a substituent at position 1 on the nitrogen atom of the indole ring, which is a very specific position, he would always consider the substituents proposed by Filla et al for this position, and no others. There is no reason to ignore the substituents proposed by Filla et al, and take instead the substituent that is at position 3 in Merce-Vidal et al.

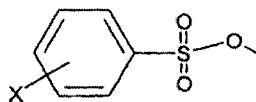
It is also important to note that the substituents of a chemical compound may not be interpreted in isolation. In the present case, the general formula of the indole derivatives disclosed in Filla et al have two additional substitutions clearly unrelated to the compounds of the present invention, namely:

- Position 3 of the indole derivatives of the present invention does not allow an heterocyclic moiety other than an heteroaryl radical, which implies aromaticity. On the contrary, in Filla et al the moiety



is mandatory in position 3 of the indole ring, as stated in the general formula (I) of said application.

- Position 5 of the indol-5-yl sulfonamide derivatives of the present invention is always substituted by a sulfonamide moiety, whereas said position is necessary substituted by a sulfonic acid moiety in Filla et al, as stated in the general formula (I) of the application, concretely by the following moiety



Unexpectedly superior properties over the prior art

Further, the Examiner contends that there is nothing in record to indicate that the instantly claimed compound possesses any unexpectedly superior properties over the prior art compound taught by Merce-Vidal et al such as, for example, reduced toxicity (as in *Takeda*) to overcome this *prima facie* rejection.

Appellants state that before comparing the properties of the claimed and the prior art compounds, the *prima facie* rejection requires finding in the prior art any reason that would have led a skilled artisan to modify the compounds disclosed in Merce-Vidal et al in the manner necessary to arrive at the claimed compounds.

Merce-Vidal et al, taken alone, fails to provide any hint to move the amino moiety or the *N*-containing cycloaliphatic ring to the 1-position of the indole ring without losing affinity for the 5-HT₆ receptor. Filla et al does not suggest to change the $-(CH_2)_n-R^2$ moiety of Merce-Vidal et al to position 1 either.

Further, it should be noted that Filla et al contains several synthetic examples and tests which can be carried out to evaluate the compounds disclosed therein but no concrete

result to these tests of at least one compound. Accordingly, it is doubtful that the skilled artisan from Filla et al would consider ring-walking the moiety to position 1 of the indole core with the reasonable expectation that compounds possessing such modification would still function as 5-HT₆ modulators.

Positional isomers

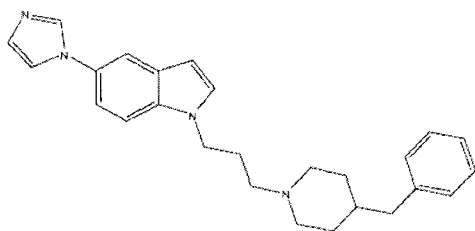
The shift of $-(CH_2)_n-R^1$ from position 3 on the indole ring (as in Merce-Vidal et al) to position 1 on the indole ring (as in the instant application) is not irrelevant. Examiner's attention is drawn to MPEP 2144.09 which states:

*“Compounds which are position isomers (compounds having the same radicals in physically different positions on the same nucleus) or homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by $-CH_2-$ groups) are **generally** of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. In re Wilder 563 F.2d 457, 195 USPQ 426 (CCPA 1977).”* (emphasis added)

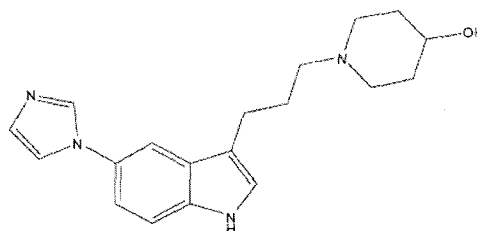
Thus, even it were the case that the claimed compounds are simply position isomers or homologs of the compounds disclosed by Merce-Vidal et al Appellants, who would bear the burden of proof, have provided bibliographic evidences in the response filed on November 28, 2008 to prove that the different biological properties between 1-substituted and 3-substituted indoles are known from the prior art. The documents provided (WO 93/20065 vs Russell, M.G.; *J. Med. Chem.*; (1999); 42(24); 4981-5001; Liou, J.P.; *J. Med. Chem.*; (2007); 50(18); 4548-4552 vs Leonard, B.E.; *Neuropharmacology*; (1972); 11(3); 373-384) show how such positional isomers not only can have a different activity regarding the same receptor, but also their activity can be associated with different receptors, which implies totally different medical uses.

Specifically, Merce-Vidal et al provides no hint as to moving the amino moiety or the N-containing cycloaliphatic ring to the 1-position of the indole ring without losing affinity for the 5-HT₆ receptor.

In addition, the Examiner's assertions do not stand comparison with similar situations described in the state of the art. For example, compound (1) is claimed as inhibitor of thromboxane A₂ synthesis in WO 93/20065, while compound (2), having a similar substituent but in position 3, is described as highly selective h5-HT_{1D} receptor agonist in Russell, M.G.; *J. Med. Chem.*; (1999); 42(24); 4981-5001.

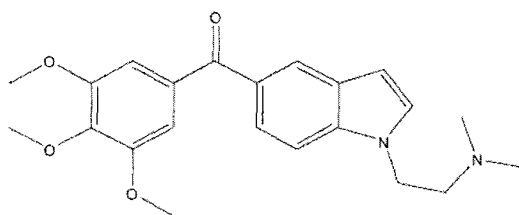


Compound (1)

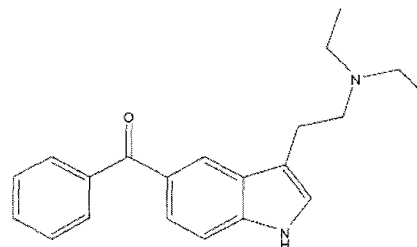


Compound (2)

A similar situation arises when comparing compound (5), which is described as potent antitubulin agent in Liou, J.P.; *J. Med. Chem.*; (2007); 50(18); 4548-4552, with compound (6) of Leonard, B.E.; *Neuropharmacology*; (1972); 11(3); 373-384, which is described as having effects on brain monoamines and their precursor amino acids.



Compound (5)



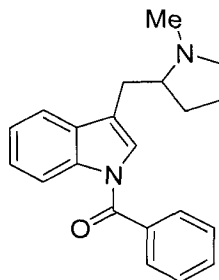
Compound (6)

Thus, the skilled artisan considering Merce-Vidal et al in light of the prior art, could expect changing the $-(CH_2)_n-R^2$ moiety to position 1 to have dramatic changes in the

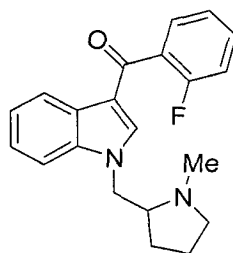
properties of the resulting compounds. Neither Merce-Vidal et al nor Filla et al provide any reasonable basis to conclude that making the substitutions and modifications to the compound disclosed by Merce-Vidal et al based on Filla et al would have similar activity.

Despite the foregoing, the Examiner alleged that this showing is not persuasive because none of the compounds referenced is drawn to modulators of 5-HT₆. Even though Appellants maintain that the foregoing is germane to the question at hand, they provided an example of two different compounds that can be associated with a “positional isomerism” for which US patents have been granted: one of them proposed as 5-HT₆ antagonist and the other proposed for treating intraocular pressure or glaucoma, which are not related to 5-HT₆ receptor. Such compounds are respectively:

- RN: 244122-12-1 US 6,100,291 granted on August 8, 2000;



- RN: 137642-51-4 US 5,607,933 granted on April 3, 1997.



As complementary note, it is remarkable that 244122-12-1, which has a tryptamine-like structure (as Filla et al, a 3-aminocycloalkylindole structure (i.e. a tertiary amine), acts as 5-HT₆ antagonist whereas when the pyrrolidinalkyl moiety is moved to position 1 (137642-

51-4), the compound is indicated for disorders not related to said receptor such as the reduction of intraocular pressure.

Nevertheless, the Examiner didn't find persuasive this argument either because although it is clear that the referenced compounds are known to have different activities, it is not clear that the compounds also lack the same activity. Further, the Examiner points that the compounds differ in more respects than the present case and it would be impossible to ascertain the reason of the difference in activity.

Appellants agree that the fact that one positional isomer possesses affinity for a receptor X and other positional isomer binds to receptor Y does not prevent, in itself, that the first isomer shows affinity for the receptor Y as well. However, such a reasoning is merely speculative and therefore the skilled artisan would only readily understand from the referenced examples that positional isomers may show very different activities.

Thus, a person skilled in the art considering Merce-Vidal et al in light of the prior art, could expect changing the $-(CH_2)_n-R^2$ moiety to position 1 to have dramatic changes in the properties of the resulting compounds.

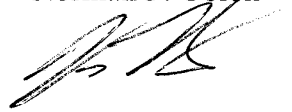
In view of the foregoing, Appellants submit that the combined disclosures of Merce-Vidal et al taken with Filla et al fail to support a *prima facie* case of obviousness. Accordingly, it is respectfully requested that this rejection be REVERSED.

VIII. CONCLUSION

For the above reasons, Claims 1-14, 18-19, 46-47, 74-82, 84-90, and 92-93 are patentable over Merce-Vidal et al taken with Filla et al. Therefore, the Examiner's rejection should be REVERSED.

Respectfully submitted,

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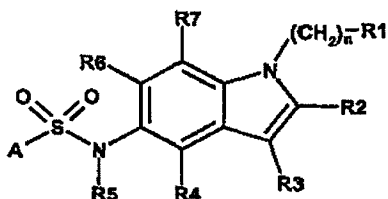
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Attachments: Claims Appendix:
Evidence Appendix
Related Proceedings Appendix

CLAIMS APPENDIX

Claims involved in this Appeal of U.S. Application Serial No. 10/566,094

Claim 1: A sulfonamide compound of general formula (Ia)



(Ia)

wherein

R¹ represents an -NR⁸R⁹ radical or a saturated or unsaturated, optionally at least mono-substituted, cycloaliphatic radical, which may optionally contain at least one heteroatom as a ring member and/or which may be condensed with a saturated or unsaturated, optionally at least mono-substituted mono- or bicyclic cycloaliphatic ring system, which may optionally contain at least one heteroatom as a ring member,

R², R³, R⁴, R⁶ and R⁷, identical or different, each represent hydrogen, halogen, nitro, alkoxy, cyano, a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical or an optionally at least mono-substituted phenyl radical or an optionally at least mono-substituted heteroaryl radical,

R⁵ represents hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

R⁸ and R⁹, identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

with the proviso that R⁸ and R⁹ are not hydrogen at the same time, and if one of them, R⁸ and R⁹, represents a saturated or unsaturated, linear or branched, optionally at least mono-

substituted C₁-C₄ aliphatic radical, the other one represents a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical with at least five carbon atoms, or

R⁸ and R⁹ together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted heterocyclic ring, which may contain at least one additional heteroatom as a ring member and/or which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, mono- or bicyclic cycloaliphatic ring system which may optionally contain at least one heteroatom as a ring member,

A represents an optionally at least mono-substituted mono- or polycyclic aromatic ring system, which may be bonded via an optionally at least mono-substituted alkylene, alkenylene or alkynylene group and/or which may contain at least one heteroatom as a ring member in one or more of its rings,

and

n is 0, 1, 2, 3 or 4;

optionally in form of one of its stereoisomers, its racemate or in form of a mixture of at least two of its stereoisomers, in any mixing ratio, or a salt thereof.

Claim 2: A compound according to claim 1, wherein R¹ represents an -NR⁸R⁹ radical or a saturated or unsaturated, optionally at least mono-substituted 5- or 6-membered cycloaliphatic radical which may optionally contain at least one heteroatom as a ring member and/or which may be condensed with a saturated or unsaturated, optionally at least mono-substituted mono- or bicyclic cycloaliphatic ring system, which may optionally contain at least one heteroatom as a ring member, whereby the rings of the ring system are 5- or 6-membered.

Claim 3: A compound according to claim 1, wherein R^2 , R^3 , R^4 , R^6 and R^7 , identical or different, each represent hydrogen, a linear or branched, optionally at least mono-substituted C_1 - C_6 alkyl radical, a linear or branched, optionally at least mono-substituted C_2 - C_6 alkenyl radical or a linear or branched, optionally at least mono-substituted C_2 - C_6 alkynyl radical.

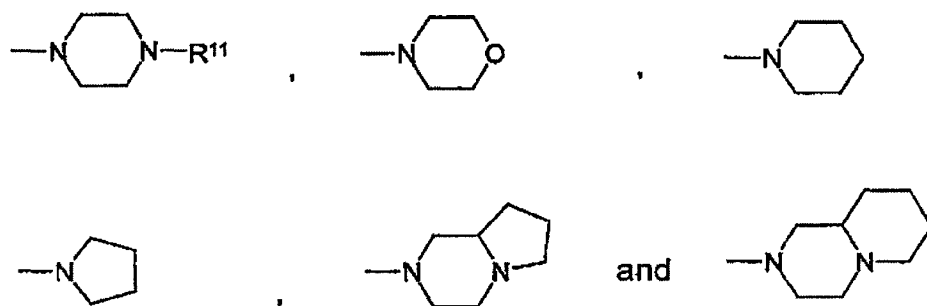
Claim 4: A compound according to claim 1, wherein R^5 represents hydrogen, a linear or branched, optionally at least mono-substituted C_1 - C_6 alkyl radical, a linear or branched, optionally at least mono-substituted C_2 - C_6 alkenyl radical, a linear or branched, optionally at least mono-substituted C_2 - C_6 alkynyl radical.

Claim 5: A compound according to claim 1, wherein R^8 and R^9 , identical or different, each represent hydrogen, a linear or branched, optionally at least mono-substituted C_1 - C_{10} alkyl radical, a linear or branched, optionally at least mono-substituted C_2 - C_{10} alkenyl radical, a linear or branched, optionally at least mono-substituted C_2 - C_{10} alkynyl radical,

or

R^8 and R^9 together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted 5- or 6-membered heterocyclic ring which may contain at least one additional heteroatom as a ring member and/or which may be condensed with a saturated or unsaturated, optionally at least mono-substituted mono- or bicyclic cycloaliphatic ring system, which may optionally contain at least one heteroatom as a ring member, whereby the rings of the ring system are 5, 6- or 7-membered.

Claim 6: A compound according to claim 5, wherein R^8 and R^9 , identical or different, each represent hydrogen or a linear or branched C_1 - C_{10} alkyl radical, or R^8 and R^9 together with the bridging nitrogen atom form a radical chosen from the group consisting of



wherein R^{11} , if present, represents hydrogen, a linear or branched C_1 - C_6 alkyl radical or a benzyl radical.

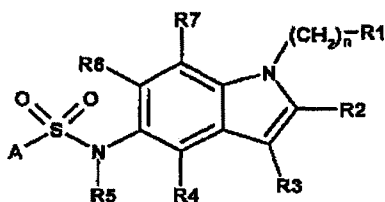
Claim 7: A compound according to claim 1, wherein A represents an optionally at least mono-substituted mono- or polycyclic aromatic ring system, wherein the ring(s) is/are 5- or 6-membered, which may be bonded via an optionally at least mono-substituted C_1 - C_6 alkylene group, an optionally at least mono-substituted C_2 - C_6 alkenylene group or an optionally at least mono-substituted C_2 - C_6 alkynylene group and/or wherein the ring(s) may contain at least one heteroatom as a ring member.

Claim 8: A compound according to claim 1 chosen from the group consisting of

- [16] N-[1-(2-pyrrolidine-1-yl-ethyl)-1H-indole-5-yl]-naphthalene-2-sulfonamide,
- [17] N-[1-(2-pyrrolidine-1-yl-ethyl)-1H-indole-5-yl]-naphthalene-1-sulfonamide,
- [18] N-[1-(2-pyrrolidine-1-yl-ethyl)-1H-indole-5-yl]-5-chloro-3-methylbenzo[b]thiophene-2-sulfonamide,

- [28] N-[1-(2-pyrrolidine-1-yl-ethyl)-1H-indole-5-yl]-6-chloroimidazo[2,1-b]thiazole-5-sulfonamide,
- [43] 5-chloro-3-methyl-N-(1-(3-(piperidin-1-yl)propyl)-1H-indol-5-yl)benzo[b]thiophene-2-sulfonamide,
- [44] N-(1-(3-(piperidin-1-yl)propyl)-1H-indol-5-yl)naphthalene-2-sulfonamide,
- [45] N-(1-(3-(piperidin-1-yl)propyl)-1H-indol-5-yl)naphthalene-1-sulfonamide,
- [46] 6-chloro-N-(1-(3-(piperidin-1-yl)propyl)-1H-indol-5-yl)imidazo[2,1-b]thiazole-5-sulfonamide,
- [47] 4-phenyl-N-(1-(3-(piperidin-1-yl)propyl)-1H-indol-5-yl)benzenesulfonamide,
- [48] 2-(naphth-1-yl)-N-(1-(3-(piperidin-1-yl)propyl)-1H-indol-5-yl)ethanesulfonamide,
- [49] 4-phenoxy-N-(1-(3-(piperidin-1-yl)propyl)-1H-indol-5-yl)benzenesulfonamide,
- [50] 3,5-dichloro-N-(1-(3-(piperidin-1-yl)propyl)-1H-indol-5-yl)benzenesulfonylamide,
- [51] 4,5-dichloro-N-(1-(3-(piperidin-1-yl)propyl)-1H-indol-5-yl)thiophene-2-sulfonamide and
- [52] 5-chloro-N-(1-(3-(piperidin-1-yl)propyl)-1H-indol-5-yl)naphthalene-1-sulfonamide,
- and their corresponding salts.

Claim 9: A sulfonamide compound of general formula (Ib)



(Ib)

wherein

R¹ represents a -NR⁸R⁹ radical,

R², R³, R⁴, R⁶ and R⁷, identical or different, each represent hydrogen, halogen, nitro, alkoxy, cyano, a saturated or unsaturated, optionally at least mono-substituted, linear or branched aliphatic radical, or an optionally at least mono-substituted phenyl or an optionally at least mono-substituted heteroaryl radical,

R⁵ represents hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

R⁸ and R⁹, identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted, C₁-C₄ aliphatic radical,

A represents an optionally at least mono-substituted mono- or polycyclic aromatic ring system, which may be bonded via an optionally at least mono-substituted alkylene, alkenylene or alkynylene group and/or which may contain at least one heteroatom as a ring member in one or more of its rings,

and n is 0, 1, 2, 3 or 4;

optionally in form of one of its stereoisomers its racemate or in form of a mixture of at least two of its stereoisomers, in any mixing ratio, or a salt thereof.

Claim 10: A compound according to claim 9, wherein R^2 , R^3 , R^4 , R^6 and R^7 , identical or different, each represent hydrogen, a linear or branched, optionally at least mono-substituted C_1 - C_6 alkyl radical, a linear or branched, optionally at least mono-substituted C_2 - C_6 alkenyl radical, or a linear or branched, optionally at least mono-substituted C_2 - C_6 alkynyl radical.

Claim 11: A compound according to claim 9, wherein R^5 represents hydrogen, a linear or branched, optionally at least mono-substituted C_1 - C_6 alkyl radical, a linear or branched, optionally at least mono-substituted C_2 - C_6 alkenyl radical or a linear or branched, optionally at least mono-substituted C_2 - C_6 alkynyl radical.

Claim 12: A compound according to claim 9 wherein R^8 and R^9 , identical or different, each represent hydrogen or a linear or branched, optionally at least mono-substituted C_1 - C_4 alkyl radical,

with the proviso that R^8 and R^9 are not hydrogen at the same time.

Claim 13: A compound according to claim 9 wherein A represents an optionally at least mono-substituted mono- or polycyclic aromatic ring system, wherein the ring(s) is/are 5- or 6-membered, which may be bonded via an optionally at least mono-substituted C_1 - C_6 alkylene group, an optionally at least mono-substituted C_2 - C_6 alkenylene group or an optionally at least mono-substituted C_2 - C_6 alkynylene group and/or wherein the ring(s) may contain at least one heteroatom as a ring member.

Claim 14: A compound according to claim 9 selected from the group consisting of

- [1] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-5-chloro-3-methylbenzo[b]thiophene-2-sulfonamide,
- [2] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-naphthalene-2-sulfonamide,
- [3] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-naphthalene-1-sulfonamide,
- [4] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-5-chloronaphthalene-1-sulfonamide,
- [5] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-benzenesulfonamide,
- [6] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-quinoline-8-sulfonamide,
- [7] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-4-phenoxybenzenesulfonamide,
- [8] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-4-methylbenzenesulfonamide,
- [9] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-5-chlorothiophene-2-sulfonamide,
- [10] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-benzo[1,2,5]thiadiazole-4-sulfonamide,
- [11] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-6-chloroimidazo[2,1-b]thiazole-5-sulfonamide,
- [12] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-3,5-dichlorobenzenesulfonamide,
- [13] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-3-bromobenzenesulfonamide,
- [14] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-3-nitrobenzenesulfonamide,
- [15] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-1-phenylmethanesulfonamide,
- [19] trans-N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-2-phenylethanesulfonamide,

- [20] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-4,5-dichlorothiophene-2-sulfonamide,
- [21] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-4-acetylbenzenesulfonamide,
- [22] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-4-bromobenzenesulfonamide,
- [23] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-4-methoxybenzenesulfonamide,
- [24] N-[1-(2-diethylaminoethyl)-1H-indole-5-yl]-5-chloro-3-methylbenzo[b]thiophene-2-sulfonamide,
- [25] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-4-nitrobenzenesulfonamide,
- [26] N-[1-(2-dimethylaminoethyl)-1H-indole-5-yl]-4-fluorobenzenesulfonamide,
- [27] N-[1-(2-diethylaminoethyl)-1H-indole-5-yl]-6-chloroimidazo[2,1-b]thiazole-5-sulfonamide,
- [29] N-(1-(2-(diethylamino)ethyl)-1H-indol-5-yl)-naphthalene-2-sulfonamide,
- [30] N-(1-(2-(diethylamino)ethyl)-1H-indol-5-yl)-naphthalene-1-sulfonamide,
- [31] N-(1-(2-(diethylamino)ethyl)-1H-indol-5-yl)-4-phenylbenzenesulfonamide,
- [32] 5-chloro-N-(1-(2-(dimethylamino)ethyl)-2-methyl-1H-indol-5-yl)-3-methylbenzo[b]thiophene-2-sulfonamide,
- [33] N-(1-(2-(dimethylamino)ethyl)-2-methyl-1H-indol-5-yl)-naphthalene-2-sulfonamide,
- [34] N-(1-(2-(dimethylamino)ethyl)-2-methyl-1H-indol-5-yl)-naphthalene-1-sulfonamide,
- [35] 6-chloro-N-(1-(2-(dimethylamino)ethyl)-2-methyl-1H-indol-5-yl)imidazo[2,1-b]thiazole-5-sulfonamide,
- [36] N-(1-(2-(dimethylamino)ethyl)-2-methyl-1H-indol-5-yl)-4-phenylbenzenesulfonamide,

- [37] N-(1-(2-dimethylamino)ethyl)-2-methyl-1H-indol-5-yl)-2-(naphth-1-yl)-ethanesulfonamide,
- [38] N-(1-(2-(dimethylamino)ethyl)-2-methyl-1H-indol-5-yl)-4-phenoxybenzenesulfonamide,
- [39] 3,5-dichloro-N-(1-(2-(dimethylamino)ethyl)-2-methyl-1H-indol-5-yl)-benzenesulfonamide,
- [40] N-(1-(2-(dimethylamino)ethyl)-2-methyl-1H-indol-5-yl)benzo[b]thiophene-3-sulfonamide,
- [41] N-(1-(2-(diethylamino)ethyl)-1H-indol-5-yl)benzo[b]thiophene-3-sulfonamide
and
- [42] N-(1-(2-(dimethylamino)ethyl)-1H-indol-5-yl)benzo[b]thiophene-3-sulfonamide,
- and their corresponding salts.

Claims 15 - 17 (Canceled):

Claim 18: A pharmaceutical composition comprising a therapeutically effective amount of at least one compound according to claim 1 and optionally at least one or more of pharmacologically acceptable excipients.

Claim 19: A pharmaceutical composition according to claim 18, for 5-HT₆ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), for the prophylaxis and/or treatment of

gastrointestinal tract disorders, for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, schizophrenia, psychosis or infantile hyperkinesia (ADHD, attention deficit/hyperactivity disorder).

Claims 20 - 45 (Canceled):

Claim 46: A pharmaceutical composition comprising a therapeutically effective amount of at least one compound according to claim 9 and optionally at least one or more of pharmacologically acceptable excipients.

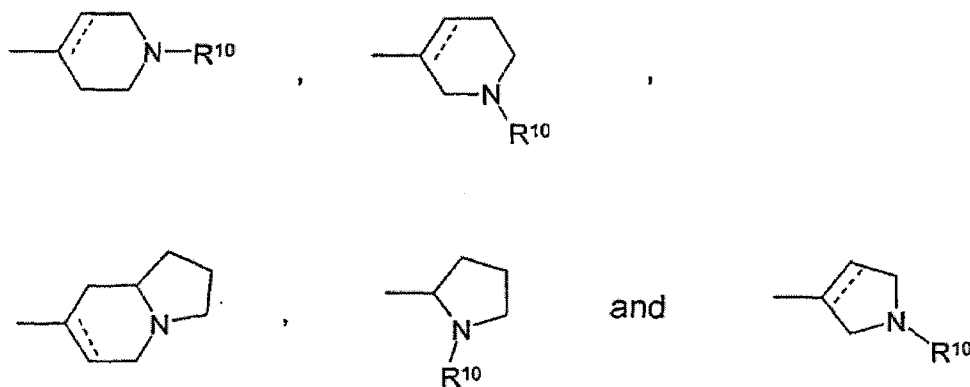
Claim 47: A pharmaceutical composition according to claim 46 for 5-HT₆ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), for the prophylaxis and/or treatment of gastrointestinal tract disorders, for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, , psychosis or infantile hyperkinesia (ADHD, attention deficit/hyperactivity disorder).

Claims 48 - 73 (Canceled):

Claim 74: The compound according to claim 1, wherein the compound is in the form of a physiologically acceptable salt thereof.

Claim 75: the compound according to claim 1, wherein the compound is in the form of its enantiomers or diastereomers or in the form of a mixture of at least two of its enantiomers and/or diastereomers.

Claim 76: The compound according to claim 2, wherein R^1 represents an $-NR^8R^9$ radical or a radical chosen from the group consisting of



wherein, if present, the dotted line is an optional chemical bond, and R^{10} represents hydrogen, a linear or branched C_1 - C_6 alkyl radical or a benzyl radical.

Claim 77: The compound according to claim 76, wherein R^{10} is hydrogen or a C_1 - C_2 alkyl radical.

Claim 78: The compound according to claim 3, wherein R^2 , R^3 , R^4 , R^6 and R^7 , identical or different, each represent hydrogen or a linear or branched, optionally at least mono-substituted C_1 - C_6 alkyl radical.

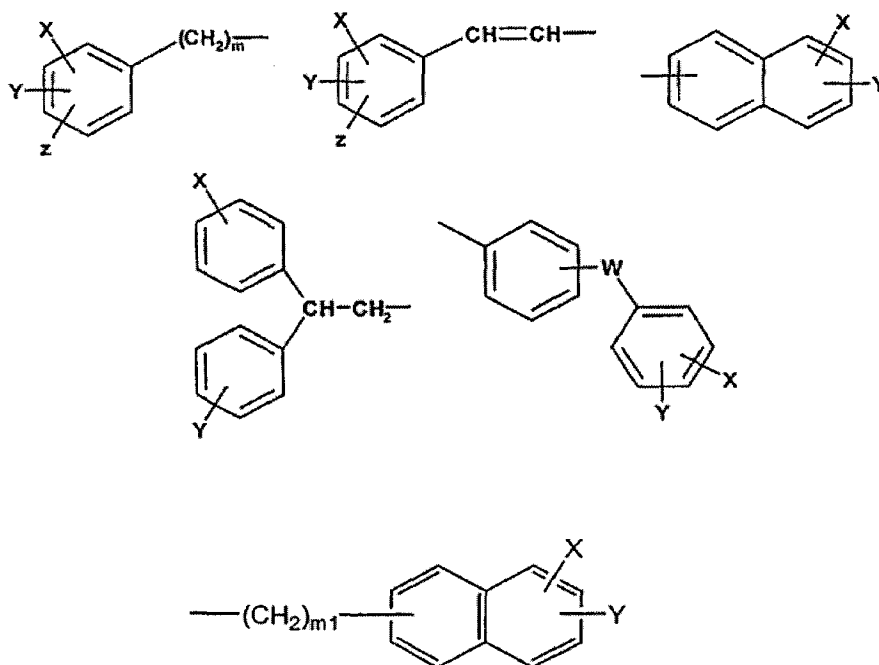
Claim 79: The compound according to claim 78, wherein R^2 , R^3 , R^4 , R^6 and R^7 each represent hydrogen or a C_1 - C_2 alkyl.

Claim 80: The compound according to claim 4, wherein R^5 represents hydrogen or a linear or branched, optionally at least mono-substituted C_1 - C_6 alkyl radical.

Claim 81: The compound according to claim 80, wherein R^5 represents hydrogen or a C_1 - C_2 alkyl radical.

Claim 82: The compound according to claim 6, wherein R^{11} represents hydrogen or a C_1 - C_2 alkyl radical.

Claim 83: The compound according to claim 7, wherein A represents an optionally at least mono-substituted mono- or polycyclic aromatic ring system, wherein the ring(s) is/are 5- or 6-membered and wherein one or more of the rings contain at least one heteroatom, or a radical chosen from the group consisting of



wherein X, Y, Z, independently from one another, each represent a radical selected from the group consisting of hydrogen, fluorine, chlorine, bromine, nitro, acetyl, linear or branched C_1 - C_6 alkyl, linear or branched C_1 - C_6 alkoxy, linear or branched C_1 - C_6 alkylthio, a trifluoromethyl radical, a cyano radical and a $-NR^{12}R^{13}$ radical,

wherein R^{12} and R^{13} , identical or different, each represent hydrogen or linear or branched C_1 - C_6 alkyl,

W represents a single chemical bond between the two rings, a CH_2 , O, S group or a NR^{14} radical,

wherein R^{14} is hydrogen or a linear or branched C_1 - C_6 alkyl,

m is 0, 1, 2, 3 or 4 and

m_1 is 1 or 2.

Claim 84: The compound according to claim 9, wherein the salt is in the form of a physiologically acceptable salt thereof.

Claim 85: The compound according to claim 9, wherein the compound is in the form of its enantiomers or diastereomers, or in the form of a mixture of at least two of its enantiomers and/or diastereomers.

Claim 86: The compound according to claim 10, wherein R^2 , R^3 , R^4 , R^6 and R^7 , identical or different, each represent hydrogen or a linear or branched, optionally at least mono-substituted C_1 - C_6 alkyl radical.

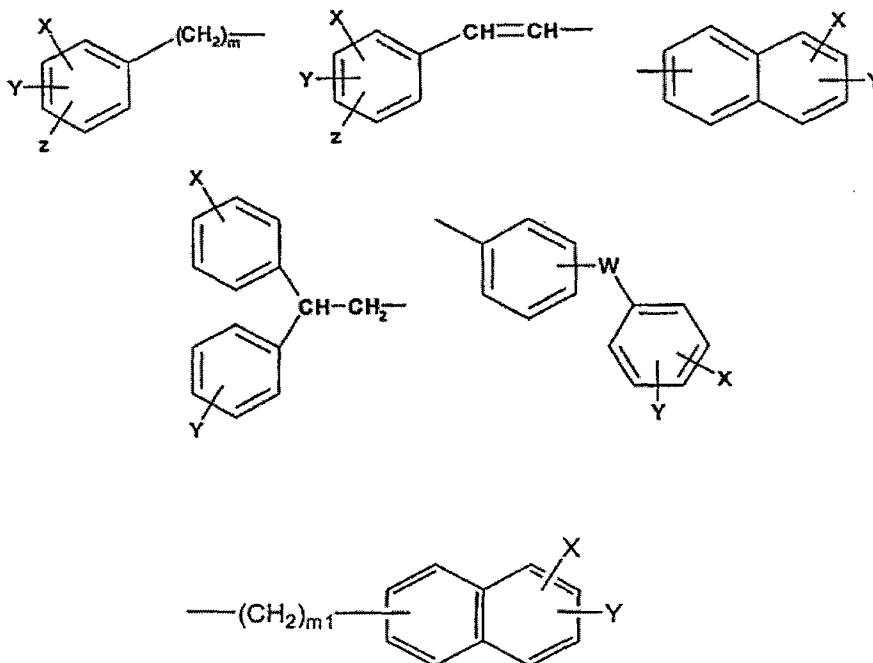
Claim 87: The compound according to claim 86, wherein R^2 , R^3 , R^4 , R^6 and R^7 each represent hydrogen or a C_1 - C_2 alkyl.

Claim 88: The compound according to claim 11, wherein R^5 represents hydrogen or a linear or branched, optionally at least mono-substituted C_1 - C_6 alkyl radical.

Claim 89: The compound according to claim 88, wherein R^5 represents hydrogen or a C_1 - C_2 alkyl radical.

Claim 90: The compound according to claim 12, wherein R^8 and R^9 , identical or different, each represent hydrogen or a C_1 - C_2 alkyl radical.

Claim 91: The compound according to claim 13, wherein A represents an optionally at least mono-substituted mono- or polycyclic aromatic ring system, wherein the ring(s) is/are 5- or 6-membered and wherein one or more of the rings contain at least one heteroatom, or a radical chosen from the group consisting of



wherein X, Y, Z, independently from one another, each represent a radical selected from the group consisting of hydrogen, fluorine, chlorine, bromine, nitro, acetyl, linear or branched C_1 - C_6 alkyl, linear or branched C_1 - C_6 alkoxy, linear or branched C_1 - C_6 alkylthio, a trifluoromethyl radical, a cyano radical and a $-NR^{12}R^{13}$ radical,

wherein R^{12} and R^{13} , identical or different, each represent hydrogen or linear or branched C_1 - C_6 alkyl,

W represents a single chemical bond between the two rings, a CH_2 , O, S group or a NR^{14} radical,

wherein R^{14} is hydrogen or a linear or branched C_1 - C_6 alkyl,

m is 0, 1, 2, 3 or 4 and

m1 is 1 or 2.

Claim 92: A pharmaceutical composition according to claim 19, wherein the disorder or disease related to food intake is selected from the group consisting of regulation of appetite, the maintenance, increase or reduction of body weight; the type II diabetes is selected from type II diabetes caused by obesity; the gastrointestinal tract disorder is irritable bowel syndrome; and the neurodegenerative disorders are selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease and/or multiple sclerosis.

Claim 93: A pharmaceutical composition according to claim 47, wherein the disorder or disease related to food intake is selected from the group consisting of regulation of appetite, the maintenance, increase or reduction of body weight; the type II diabetes is selected from type II diabetes caused by obesity; the gastrointestinal tract disorder is irritable bowel syndrome; and the neurodegenerative disorders are selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease and/or multiple sclerosis.

EVIDENCE APPENDIX

- 1) Sophie-Isabelle Bascop et al., *Arkivoc* **2003** 46-61, 2(3) as originally filed on June 23, 2009.
- 2) Yuching Tsai et al., “N1-(Benzenesulfonyl)tryptamines as novel 5-HT6 antagonists”, *Bioorganic & medicinal chemistry letters* **2000**, vol. 10, no 20, pp. 2295-2299 as originally filed on June 23, 2009.
- 3) Richard A. Glennon et al., “2-Substituted Tryptamines: Agents with Selectivity for 5-HT6 Serotonin Receptors”, *J. Med. Chem.*, **2000**, 43 (5), pp 1011–1018 as originally filed on June 23, 2009.
- 4) WO 93/20065 as originally filed on November 28, 2008.
- 5) Russell, M.G.; *J. Med. Chem.*; **(1999)**; 42(24); 4981-5001 as originally filed on November 28, 2008.
- 6) Liou, J.P.; *J. Med. Chem.*; **(2007)**; 50(18); 4548-4552 as originally filed on November 28, 2008.
- 7) Leonard, B.E.; *Neuropharmacology*; **(1972)**; 11(3); 373-384 as originally filed on November 28, 2008.

RELATED PROCEEDINGS APPENDIX

None.